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CORRELATION BETWEEN SERUM INFLAMMATORY BIOMARKERS AND COVID-19 SEVERITY

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Abstract

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a global health crisis with a wide spectrum of clinical manifestations ranging from mild respiratory symptoms to severe pneumonia, multi-organ dysfunction, and death. Inflammatory biomarkers have been identified as valuable indicators for assessing disease severity, as they reflect the host immune response to infection. Monitoring these biomarkers can provide important insights into disease progression and guide clinical management. This study investigated the correlation of inflammatory biomarkers in COVID-19 patients and their differential patterns across mild to severe disease. Medical records of 100 confirmed cases admitted to the isolation ward of Rahman Medical Institute (RMI), Peshawar, between May and August 2020 were retrospectively reviewed. All patients had tested positive for SARS-CoV-2 RNA by RT-PCR on nasopharyngeal swabs. Laboratory investigations included lactate dehydrogenase (LDH), C-reactive protein (CRP), D-dimer, and ferritin, performed at the RMI Laboratory. The results revealed elevated levels of these biomarkers, with CRP showing the highest frequency of elevation, observed in up to 78% of cases. Ferritin was abnormal in 66% of patients, D-dimer in 76%, and LDH in 83%, while the remaining percentages represented patients with normal levels. These findings demonstrate that elevations in inflammatory biomarkers are strongly correlated with disease severity in COVID-19 patients.

INTRODUCTION

Coronavirus disease 2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has emerged as a global health crisis with a wide spectrum of clinical manifestations ranging from mild respiratory symptoms to severe pneumonia, multi-organ dysfunction, and death. Inflammatory biomarkers have been identified as valuable indicators for assessing disease severity, as they reflect the host immune response to infection. Monitoring these biomarkers can provide important insights into disease progression and guide clinical management.

Late in 2019, a virus, named as severe acute respiratory syndrome corona virus 2(SARS-CoV-2), spread over globally from the city of Wuhan, China, as the causative agent of the acute severe respiratory syndrome. According to the world health organization (WHO) this novel virus as a pandemic on March 11 2020. Clinical sign and symptoms of this viral disease are showed much similar to pneumonia caused by viruses. The outbreak of nCOVID-19 in China and its

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global outreach led to the WHO to declare it as a Public Health Emergency on January 2020 [1].

The causative Pathogen is recognized as a singles-stranded ribonucleic acid (RNA) beta corona virus named as (SARS-CoV-2), sharing an about 79% resemblance at nucleotide level with severe acute respiratory syndrome corona virus (SARS-CoV). According to WHO, this continuing global COVID-19 pervasive has led to a massive risk to worldwide public health. In the meantime, of, 2020, 21, a total of 266,073 positive confirmed cases from a total of 150 states and regions were reported, consisting 11,183 mortalities [2].

Infection caused by the SARS-CoV-2 in lungs results in an increased vascular permeability and sub-pleural inflammation and, hence causing edema within the tissues. Increased ventilation, tidal volume, and rate of respiration are physiological responses of the body to the lower levels of oxygen. Hypoxemia, with an increased rate of metabolism resulted due to inflammation, fever, and elevated oxygen consumption adds up an increase in the respiratory rate. A careful observation of the patients is required as their condition can deteriorate quickly, and proper monitoring of inflammatory biomarkers is specifically useful in understanding the prognostic status of the patients[3].

In common, coronaviruses can lead to different clinical manifestations, including respiratory, enteric, neurological and hepatic illnesses. Serious respiratory illness can be found in patients of old age and specified groups of patients, such as patients with pre-existing medical conditions. Diagnosis at earliest is important while considering the brief time of appearance of acute respiratory syndrome at the time of admission to the hospital and high mortality rates in COVID-19[4].

Patients Infected with COVID-19 may face with some of the mentioned following symptoms; dyspnea, high fever, myalgia, high grade fever, headache, cough, production of sputum, hemoptysis, and diarrhea, while in several cases, ARDS, secondary infection and cardiac injury. Till date, more than 198 countries had been influenced by the disease of COVID-19 with more than 03 million confirmed positive effected cases resulting in more than 200,000 causalities. But still many more remain un-highlighted or unreported in different territories worldwide[5].

Acute inflammation in sub-pleural areas of the lungs is a complex mechanism of pathophysiological nature which involves inflammatory mediator's like chemokines cytokines, stimulating the white blood cells (macrophages) within the alveoli, resulting in poorly regulated cellular immunity. Considering its considerations within humans, the clinical onset of the corona virus disease is found in three phases.

- The clinical signs and symptoms of the first phase consists fever, cough, body aches, and other infections that may associated with the increased rate due to replication process of viral genome and death of cells.
- In second phase there is conversion of IgG antibodies, during this phase, uncontrolled replication of the viral genome occurs resulting in worsening of symptoms[6].
- Transmission of SARSCoV-2 happens when an individual inhales the respiratory droplets excreted from an infected person. The incubation time before patient's exhibit illness symptoms is from 2 to 14 days. The worldwide

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outbreak of COVID-19 has many catastrophic impacts, with a major impact on the world's economic condition, also resulting in ~436,167 deaths globally as of June 15, 2020.According to World Health Organization (WHO) AS 33,502,430 confirmed cases of COVID-19 has been noted globally, consisting about 1,004,421 mortalities until September 30, 20207.

Transmission from Person-to-person and patterns of travel within the United States of America make it the most effected country with a total of COVID-19 infected patients over passing over 8.4M, including mortalities above the 200 thousand threshold, making it higher than China, as the origin of this virus was initiated from china.

In Pakistan the very first confirmed patient of COVID-19 infection was reported on February26, 2020, a student with a travel history from Iran. In October 2020, a total number of infected cases were more than 03 million, where 6,659 of the total deaths were reported. The total number of patients who recovered was 307,409 and 9,384 actives in Pakistan.

The province of Punjab was found to be the most affected with a total of 101,652 confirmed cases in which 2,310 mortalities were reported, while a total number of 97,252 patients were recovered with 4,400 active confirmed cases. It was predicted by Pueyo et al., 2020 model in mentioned study that number of infected positive cases maybe increased to more than 9 million until October, 20 2020 in the province of Punjab[8]. Transmission from one Human to another has been reported as for round about the most of the COVID-19 infections, consisting of the healthcare personnel of a medical hospital. Many of the patients infected from COVID-19 are non-severe patients and their symptoms are usually mild. But, the symptoms in 10% COVID-19 infected patients are considered as more severe while several lead rapidly to serious conditions, like dysfunction of organ, ARDS, cardiac injury, acute injury of kidney and death[9]. About, 14% patients infected with COVID-19 resulted in the progression of a severe form of disease with complicated manifestations such as respiratory distress syndrome, respiratory failure, acute injury of the liver and injury of the kidney, complications of cardiovascular system and failure many vital organs. People of older ages and patients with underlying conditions like diabetes, respiratory diseases, diseases of cardiovascular system, and patients with compromised immune system have a higher risk of progression into severe form of disease. Diagnosis depends on PCR testing of RNA viral nasopharyngeal samples. Other investigations are used to monitor and asses the patient's evaluation and to highlight the possible severe manifestations of the disease like complete blood Picture, C reactive protein, D-Dimer, and lactate dehydrogenase .[10] Currently RT-PCR is the topmost for the diagnosis of COVID-19. However, several other methods used by various point of care testing devices with usual and accurate being Loop Mediated Isothermal Amplification (LAMP) in a closed tube with detection being colorimetric and serologic methods of detecting IgM, IgG of COVID-19 by Rapid Test device[11]. As RT-PCR testing method is the gold standard for confirmation of COVID-19 diagnosis, but every healthcare organization or center has no access to the mentioned gold standard method by RT-PCR testing. it is essential then to evaluate the patient's condition as early as possible utilizing inflammatory biomarkers. Hematological and biochemical parameters are

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measured in quantity within biological blood samples of the infected patients. These markers are assessed while managing the course of several illnesses to indicate and predict the possible outcome of the pathologic condition and clinical manifestations of the patients[12].

The evidence accumulated so far suggests that an inflammatory response plays important and vital role in COVID-19 progression. Triggered due to SARS-CoV-2 fast replication and destructive damage to cells inflammatory responses release white blood cells such as macrophages, Monocytes inducing release of chemokines and cytokines. These chemical markers bring about the notice to cells of the immune system activating immune response, resulting to cytokine storms.

Many markers of the inflammatory system possess the ability to trace and predict accurate information of disease progression, severity and death. Biomarkers like Procalcitonin, Ferritin, erythrocyte sedimentation rate, C-reactive protein, and interleukin-6 have been reported as strongly associated with higher risks of developing a severe disease[13].

Biomarkers which are assessed and evaluated in thrombo-inflammation such as D-dimer, C reactive protein, high-sensitive C reactive protein, Ferritin, IL- 6, fibrinogen, and end-organ damage troponin I are associated with severity progression and death in COVID-19[14].

1.1. TRADITIONAL BIOMARKERS

1.1.1. Crp Level

CRP is a significant systemic biomarker of acute phase initiation in infection, tissue damage and inflammation, thereby working as an indicator of inflammation. A study conducted by Chen et al., (2020) reported that insignificant difference was established in CRP level between the non-severe and group of severe patients, as the mean CRP level was elevated associated with severe group compared to the non-severe group. However other studies suggested that elevated level of CRP was significantly related to severe progression in COVID-19[15].

A surprisingly high number of papers have focused on circulating CRP levels in COVID-19 patients, with multiple lines of evidence showing the prognostic value of this biomarker. Another retrospective study on 145 COVID-19 infected patients, CRP was defined as an early detector of disease severity and a suitable biomarker for guiding therapy.

Ali et al. [2021] published and suggested that the CRP level could predict disease worsening among non-severe cases, reporting a 5% risk of developing a severe course for every unit increase in the CRP level. Ali et al [2021] highlighted a study by Luo, et al., who identified independent predictors of death. CRP emerged as the best predictor with D-dimer, and platelet count[16]. Furthermore CRP play a significant role in activation of cytokine thereby contributing in the pro inflammatory cycle[17].

A study conducted demonstrated that elevation in CRP levels is significantly associated with COVID-19 severe progression and severe clinical manifestations. Another retrospective cohort study showed that the CRP level was significantly raised in 65% patients of COVID-19 at the time of admission and raised in 93.9%

of COVID-19 severe cases. All these studies suggest that CRP levels are vital biological markers to predict the severity of the COVID-19 infection[18].

1.1.2. Ferritin Level

Ferritin is an iron containing intracellular protein that found as storage form of iron cells. As this protein is found in tissue and different organs, some of it is secreted in blood carrying iron. Furthermore; Ferritin is also reactant of the acute phase which elevates in a progressive order of disease [84]. A study conducted by Chee showed an elevation in levels of Ferritin in 63% of patients of COVID-19 which may have an association with poor health outcomes[19].

Ferritin protects the body systematically against an active infection by blocking availability of iron to invaded pathogenic organism. An elevated Ferritin level in cause a hyperferritinemia like manifestation in those patients who are exposed to pathogens of higher levels. The role of Ferritin to use its value for different therapeutic treatments clinically is very significant. The level of serum Ferritin can also be characterized as biomarker to evaluate the prognosis of infection in COVID-19[20].

Ferritin is studied as marker of the iron metabolism, but its role as a marker of inflammatory response has shown its significance considering progression of COVID-19, as reported by conducted studies in this field. Ferritin is considered reactant of the acute phase, and is usually raised in any type of inflammatory responses. At very beginning days of admission to the hospital, in some of COVID-19 infected patients and observed significant association between elevation of serum Ferritin and overall rate of mortality, independent of the age factor.

Poor prognosis mainly associated with rapid and better approach to intensive, respiratory care and dialysis. Increased evidence suggests that serum Ferritin shows response of acute phase and also plays a significant role in the inflammation. For most clinical healthcare workers working on a inflammatory illnesses, levels of Ferritin are ruled as a non-specific marker in response of the acute phase, usually ignored and not assessed or evaluated in patients with acute illness. In many diseases, level of Ferritin can show much higher elevations and, but is ruled as non-specific, and such an elevation may be significant in identifying those patients who are at risk[21].

A study conducted by Chen observed a marked elevation in levels of Ferritin in 63% of patients infected from COVID-19 showing a sign poor outcome[22].

Another study conducted on hyper inflammation in early COVID-19 demonstrated elevated Ferritin levels in the first week of admission in the hospital and also these levels were used as possible outcome of the cytokine storm syndrome[23].

1.2. Coagulation Pathway Biomarkers

Coagulopathy is noticed, and elevations of D-dimer were found in 3.75 to 68.0% of the patients infected from COVID-19. Conducted researches in community acquired pneumonia, chronic obstructive pulmonary disease patients showed that level of D-dimer is elevated in cases which are severe using it as suitable prognostic inflammatory biomarker, while D-dimer of value > 1 μg/ml is ruled as a factor of risk for death in adult patients of COVID-19 infection[24].

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D-dimer and PT levels have been assessed in COVID-19 patients to establish their ability to predict a worse outcome, defined as development. Wu, et al. demonstrated PT and D-dimer levels to be significantly associated with ARDS development in a conducted cohort study including 201 infected patients. Coagulation indices were observed significantly higher in those patients who developed acute respiratory syndrome and died than in patients who survived[25].
Elevation of inflammatory markers in COVID-19 patients consist D-dimer, a primary degradation product enzymatic process of fibrin by the plasmin. Studies have shown that the risk of those patients' possessing shock and sepsis may be increasingly associated with elevated D-dimer levels[26].
Disorders of Coagulation are commonly occurring in COVID-19 infected patients, significantly in patients with severe illness. Furthermore, it is having been reported in studies conducted on a larger scale that 50% of patients in COVID-19 had elevated levels of D-dimer and FDPs. and the elevations showed as strongly associated with cases of severe cases. Additionally, a study in China, elevated levels of D-dimer of value >1μg/mL were significantly associated with hospital mortality. In addition to that, it is important to note that in a study conducted retrospectively, included 449 severe patients COVID-19 in the city of Wuhan, administration of heparin in patients with raised levels of D-dimer was associated correlated with overall survival 28-day[27].
A study conducted by Long reported that hyper coagulation maybe present in the early stage of COVID-19 infected patients. Hyper coagulation is correlated with the progression of disease. Disorder of the coagulation system results in elongated test time of Prothrombin. In those patients with COVID-19 infection, increase of PT test time is related with disease prognostic outcome.
A study conducted by Tang demonstrated that reduced levels of fibrinogen and raise test time of PT and elevated D-dimer are correlated with disseminated intravascular coagulopathy (DIC) in severe COVID-19 infected patients[28].

1.3. Immunological Markers

Markers associated with Systemic inflammation such as neutrophils, lymphocytes, platelets and relevant indices such as neutrophils to lymphocyte ratio, lymphocyte to Monocytes ratio, and platelet to lymphocyte ratio have been observed to predict systemic inflammation and can be used as prognostic markers in COVID-9 disease[29].
Among the cytokines, IL-6 has been assumed as very significant with respect to COVID-19. Different studies have observed an association between IL-6 levels and severe progression disease in COVID-19 infection. Elevated levels of IL-6 in severe COVID-19 patients were associated with the need for mechanical ventilation, damaged lungs on CT scans, and other inflammatory biomarkers, including CRP, D-dimer and Ferritin[30].

1.4. Other Non-Specific Biomarkers

Serum Amyloid A (SAA) and LDH are also associated biomarkers in COVID-19 disease. It his observed in many studies that ICU patients had remarkably elevated levels of LDH than non-ICU patients and that LDH levels correlated with the damage in tissue and CT scan scores, reflecting disease severity[31].

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LDH is used to predict the depict extent of damage to the tissue. Studies have shown that when levels of LDH do not come to normal within 48 hours of sepsis initiation may lead to the prediction of mortality[32].

LDH had the most significant and vital role in predicting COVID-19 patient survival status, consistent with previous studies. Decrease in the levels of LDH level was associated with the elimination of viral messenger RNA and resulting in shorter hospital stay, leading to better COVID-19 prognosis[33].

1.5. Organ-Specific Biomarkers

1.5.1. Cardiac Markers

Cardiac biomarkers which may play a significant role in the cardiac injury, myocardial infarction are Troponin I, NT proBNP may also show an elevation. Different researches conducted have observed that in the patients with COVID-19 illness, the prognostic role of important cardiac biomarkers such as NT proBNP and high sensitive troponin I could show a direct or indirect association with cardiac injury[34].

1.5.2. Liver Markers

The levels of liver enzymes, including transaminases and gamma glutamyl transferase (GGT), are usually elevated in COVID-19 patients. The elevation in GGT level is not followed by an elevation in the alkaline phosphatase level; thus, liver involvement in COVID-19 looks like similar to that of drug-induced injury. However, there is no such proper evidence of a correlation to disease severity, and the relevance of testing for liver indices in these patients is not confirmed[35].

The current study is based on the differential pattern of s inflammatory markers. By conducting this study, it may lead to generate tools for clinicians group the patients according to severity, predict the possible prognosis and mortality. The serum inflammatory biomarkers that we will review include, C-reactive protein, IL-6, white cell count, lactate dehydrogenase, D-Dimer, Ferritin, FDPs, platelet count and cardiac markers.

Objective

Investigate the correlation of different inflammatory biomarkers in Covid-19 confirmed patients and to know the differential patterns of the biomarkers in mild to severe forms of disease.

MATERIAL AND METHODS

1.1. Study Design and Duration

This retrospective cross-sectional study was designed whose duration was from May 2020 to August 2020 at Centre of Rahman medical Institute laboratory, Chemical Pathology Department, Rahman Medical Institute Hayatabad, Peshawar, Khyber Pakhtunkhwa. The study was conducted after the approval of Institutional Ethical Board of Rahman Medical Institute, Peshawar. The patients admitted to isolation ward of Rahman Medical Institute (Peshawar, Pakistan) between May 2020 and August 2020 and confirmed positive for testing RT-PCR of viral RNA on nasopharyngeal samples were included in the study. The laboratory inflammatory markers, including C-reactive protein, Lactate Dehydrogenase, D-dimer, and Ferritin, performed at the Chemical Pathology department of RMI Laboratory were studied in the selected patients. The time duration of this study was 04 months.

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1.2. Settings

The laboratory work for this study was done at Molecular Biology section of Rahman Medical Institute Laboratory.

1.3. Sample Size

Scanned Medical records of 100 patients admitted to the isolation ward of the hospital were scanned in the electronic archive of the hospital retrospectively.

1.4. Sampling Technique

Medical records of the 100 patients admitted to the isolation ward of the hospital were searched in the electronic software archive of the hospital with retrospective approach.

1.5. Data Analysis

Results were analysed by using MS excel 2007 and a statistical tool SPSS 22 was employed also for data analysis. Bar charts are generated in MS excel 2007 and the cross tabulation was done to find out association on SPSS 22.

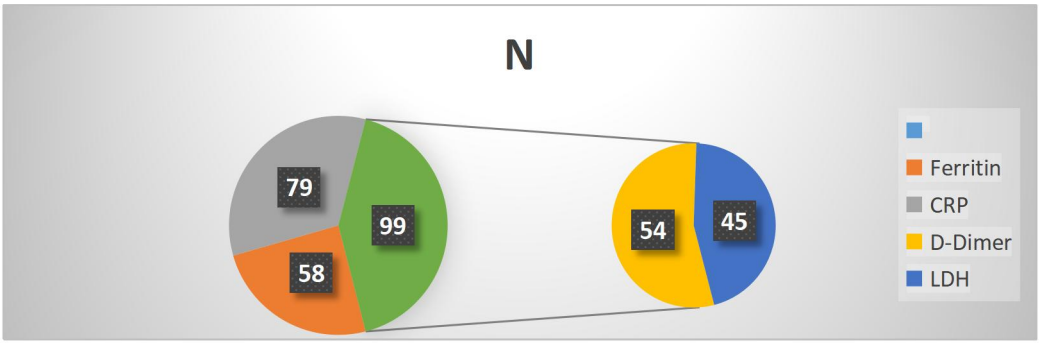
RESULTS

The current study was conducted after the approval of Institutional Ethical Board of Rahman Medical Institute, Peshawar. The patients admitted to the isolation ward of the mentioned hospital between May 2020 and August 2020 confirmed positive for RT-PCR of viral RNA on nasopharyngeal samples was included in the study. The laboratory inflammatory markers, including Lactate

CR POSITIVE CASES					
		Ferritin	**CRP**	**D-Dimer**	**LDH**
N	Valid	58	79	54	45
Mean		698.6005	4.7676	948.6852	441.2000
Std. Deviation		600.71405	7.04830	2359.06489	460.52325
Minimum		21.91	.03	.00	184.00
Maximum		2000.00	34.22	12800.00	2468.00

TABLE 3- 1: STATISTICAL ANALYSIS IS CARRIED OUT BY SAMPLE T-TEST, FREQUENCY DISTRIBUTION. THE RESULTS ARE EXPRESSED IN MEAN ±SD.

FIGURE 3- 1: PERCENTAGE OF SERUM INFLAMMATORY BIOMARKERS IN COVID-19 CONFIRMED POSITIVE CASES



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TABLE 3- 2: STATISTICAL ANALYSIS IS CARRIED OUT BY SAMPLE T-TEST, FREQUENCY DISTRIBUTION. THE RESULTS ARE EXPRESSED IN MEAN ±SD

S/No	Test Parameter	T Statistic	P-Value
1	CRP	1.44169	.151
2	Ferritin	1.62186	.109
3	LDH	0.01622	.987
4	D-Dimer	0.77806	.439

DISCUSSION

COVID-19 pandemic is one of the serious general health danger that requires quick activity. Not with the standing the extreme endeavours to discover novel medications for SARS-CoV2, this procedure is tedious with limited advancement to date. Hence, medicate repurposing has been recognized as the quickest method of figuring it out restorative specialists for COVID-19 to meet the desperation of the situation.

In the current study 100 Covid-19 patient were selected at Rahman Medical Institute a tertiary healthcare hospital Peshawar Khyber Pakhtunkhwa from May 2020 to August 2020 after taking approval of Institutional Ethical Board of Rehman Medical Institute (RMI), Peshawar. Nasopharyngeal swab collected from all patients and after confirmation by RT- PCR sample were taken from all patient for biochemical, haematological and coagulation profile in three different tubes.

The samples were then assessed in respective departments of the laboratory. Our findings were as follow: Ferritin, D-Dimer, CRP, and LDH. In this Retrospective study overall shows that among the 100 COVID-19 positive patients CRP is highly relationship 78% with inflammatory marker. Among the 100 COVID-19 positive patients the ferritin is normal in 34% of patients and abnormal in 66% patients, the D -Dimer is normal in 26% of patients and abnormal in 76 % patients, the LDH is normal in 17% of patients and abnormal in 83% patients.

The current study also shows the relationship between the Disease severity and elevation of the inflammatory biomarkers in COVID – 19.

We found that an increased level of D-dimer was correlated with a composite poor prognosis, significantly death and severe disease COVID-19. This result supports the mentioned hypothesis that SARS-CoV-2 infection could lead to the deregulation of the haemostatic body system, resulting in a hypercoagulable condition which is known as sepsis.[36, 37]

Recent studies have found the evidence of lung pathology resulted occlusion and formation of micro-thrombosis in pulmonary small vessels in patients of critical illness with the infection of COVID-19. Furthermore, raised serum D-dimer level is based on multiple factors and optimal cut-off value of raised D-dimer in COVID-19 patients still needs to be established.

It is obvious that coagulopathy associated with COVID-19- requires special emphasis along with specified treatment strategy. According to International Society of Thrombosis and Homeostasis according to guidelines, raised levels of D-dimer induces an increased thrombin production. COVID-19 Patients with raised levels of D-dimer may need hospital admission, of clinical presentation severity.[38]Another study also supports our study that dimer is degradation product of fibrin used as to exclude thrombosis diagnosis. Elevated level of D-dimer is noticed in severe cases of Covid-19 associated with microangiopathy and a state of hypercoagulability[39].

The current study shows that Serum Ferritin is very significant marker for patients with COVID-19. Furthermore, it helps in detection of the of infection severity. The study we conducted demonstrated that S. ferritin was elevated significantly in infection severity and many other studies discussed this association. Another study including 20 patients with Covid-19 having raised levels of Ferritin, reported elevated Ferritin in those patients having severe infection of Covid-19, however these levels were slightly higher in the much severe group. [40]Another research including 69 patients having severe infection of Covid-19 showed markedly elevated Ferritin levels within patients having severe form of disease than patients with non-severe group of disease.[41]

Clinically elevated levels of CRP might be of the reason as an early indicator of hospital acquired infections in patients of COVID-19 who were having a slow recovery rate. This might also help clinicians to administer antibiotics treatment earlier in the disease course to prevent any worse outcome. In the present study, a strong association between level of CRP and severity of disease was noticed.

Our study suggests that CRP has to be used as a marker of prognostic ability and raised levels of CRP associated with higher risk of disease progression. This study results consistent with the studies previously conducted which showed that hypoalbuminemia lymphopenia and CRP levels of more than or equal 40 mg/dl were the factors for prediction of Pneumonia progression resulting in respiratory distress and failure in COVID-19 infected patients.[42]

Numerous studies conducted at the time of early pandemic reported the elevated levels of LDH in severe cases or especially cases involving cardiac injury.[43, 44] As with the ongoing understanding of the COID-19 globally many several studies showed that LDH association with disease severity and prognosis of COVI-19. Another study conducted by Shi [45]reported that elevated level of LDH was a specified independent factor of risk for the exacerbation in patients with mild COVID-19. Poggiali demonstrated that high increased level of LDH might be associated with respiratory function and might be a predicting factor of respiratory failure in patients of COVID-19. Han [46]suggested that LDH could be specified a strong predicting factor for timely recognition of lung injury and severity of COVID-19 cases. All these studies are consistent with our findings.

CONCLUSIONS

In current study we demonstrated the correlation of serum inflammatory biomarkers and disease severity. Elevation of all mentioned parameters including LDH, Ferritin, CRP, and D-dimer showed strong association with disease severity and CRP was noted as the most significant acute phase reactant with its value specifically associated with evaluation of possible outcome and

prognosis. This study is helpful as elevation in inflammatory biomarkers is associated with severity of the disease; and timely monitoring by utilizing these biomarkers can significantly improve disease progression and outcome and thus could be used as significant prognostic factors of the disease.

RECOMMENDATION

To provide much improved and best clinical healthcare services all other important inflammatory biomarkers need to be studied to view their ability of prognostic capability used in the treatment of infection of COVI-19.

LIMITATIONS

Our study has certain limitations. Firstly, to analyse the severity data of only 100 patients were included retrospectively which was not enough number to establish the required research objective. This was because of unavailability of detailed information of the patient especially regarding considering the outcomes. Other important inflammatory biomarkers were also not included to assess the severity of infection properly. Another limitation was that this study was conducted at a tertiary healthcare hospital and not on a grass root platform so the exact scenario could not be visualized properly.

LIST OF ABBREVIATION

WHO	World Health Organization
CRP	C reactive Protein
LDH	Lactate Dehydrogenase
RT-PCR	Real Time reverse transcriptase polymerase chain reaction testing
IL-6	Interleukin- 6
ESR	Erythrocyte Sedimentation Rate
COVID-19	Corona Virus Disease of 2019
KP	Khyber Pakhtunkhwa
PT	Prothrombin Time
APTT	Activated Partial Thromboplastin Time

REFERENCES

1. Upadhyay J, Tiwari N, Ansari MN. Role of inflammatory markers in corona virus disease (COVID-19) patients: A review. Experimental Biology and Medicine. 2020 Sep;245(15):1368-75.
2. Zeng, Furong, et al. “Association of Inflammatory Markers with the Severity of COVID-19: A Meta-Analysis.” *International Journal of Infectious Diseases*, vol. 96, July 2020, pp. 467–74.
3. Asghar MS, Haider Kazmi SJ, Khan NA, Akram M, Jawed R, Rafaey W, et al. Role of biochemical markers in invasive ventilation of Coronavirus disease 2019 patients: Multinomial regression and survival analysis. Cureus. 2020;12(8):e10054.

4. Usul E, Şan İ, Bekgöz B, Şahin A. Role of hematological parameters in COVID-19 patients in the emergency room. Biomarkers in Medicine. 2020 Sep; 14(13):1207-15.
5. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A. The role of biomarkers in diagnosis of COVID-19–A systematic review. Life sciences. 2020 May 13:117788
6. Upadhyay J, Tiwari N, Ansari MN. Role of inflammatory markers in corona virus disease (COVID-19) patients: A review. Experimental Biology and Medicine. 2020 Sep;245(15):1368-75.
7. Akdogan D, Guzel M, Tosun D, Akpinar O. Diagnostic and early prognostic value of serum CRP and LDH levels in patients with possible COVID-19 at the first admission. J Infect Dev Ctries. 2021;15(6):766–72.
8. Saeed U, Sherdil K, Ashraf U, Mohey-Ud-Din G, Younas I, Butt HJ, et al. Identification of potential lockdown areas during COVID-19 transmission in Punjab, Pakistan. Public Health. 2021;190:42–51.
9. Wu X. Replication Data for "A cohort study of 676 patients indicates Dimerized plasmin fragment D is a critical risk factor for the mortality of COVID-19." Harvard Dataverse; 2020
10. Cai, Y.-Q., Zeng, H.-Q., Zhang, X.-B., Wei, X.-J., Hu, L., Zhang, Z.-Y., Ming, Q., Peng, Q.-P., & Chen, L.-D. (2020). Prognostic value of neutrophil-to-lymphocyte ratio, lactate dehydrogenase, D-dimer and CT score in patients with COVID-19. In *Research Square*. https://doi.org/10.21203/rs.3.rs-38585/v1
11. Ahmad S, Ali N, Kausar M, Misbah H, Wahid A. Road toward rapid-molecular point of care test to detect novel SARS-coronavirus 2019 (COVID-19): Review from updated literature. Allergologia et immunopathologia. 2020 Jul 1.
12. Akdogan D, Guzel M, Tosun D, Akpinar O. Diagnostic and early prognostic value of serum CRP and LDH levels in patients with possible COVID-19 at the first admission. J Infect Dev Ctries. 2021;15(6):766–72
13. Zeng, Furong, et al. "Association of Inflammatory Markers with the Severity of COVID-19: A Meta-Analysis." *International Journal of Infectious Diseases*, vol. 96, July 2020, pp. 467–74.
14. Chaudhary R, Garg J, Houghton DE, Murad MH, Kondur A, Chaudhary R, et al. Thromboinflammatory biomarkers in COVID-19: Systematic review and meta-analysis of 17,052 patients. Mayo Clin Proc Innov Qual Outcomes. 2021;5(2):388–402
15. Zeng, Furong, et al. "Association of Inflammatory Markers with the Severity of COVID-19: A Meta-Analysis." *International Journal of Infectious Diseases*, vol. 96, July 2020, pp. 467–74.
16. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021;41(6):540–8.
17. Das B, Bhatia SY, Pal PM. Evaluation of the role of routine laboratory biomarkers in COVID-19 patients: Perspective from a tertiary care hospital in India. Indian J Clin Biochem. 2021;1–12.
18. Hong L-Z, Shou Z-X, Zheng D-M, Jin X. The most important biomarker associated with coagulation and inflammation among COVID-19 patients. Mol Cell Biochem. 2021;476(7):2877–85.

19. Hong L-Z, Shou Z-X, Zheng D-M, Jin X. The most important biomarker associated with coagulation and inflammation among COVID-19 patients. Mol Cell Biochem. 2021;476(7):2877–85.
20. Mohan A, Padmini SN, Brunda MS, Shekhar A, Matthew P, G.R. Lingeshwaran. Role of biomarkers in predicting prognosis of Coronavirus disease 2019 (COVID-19): A retrospective cross-sectional study: Perspective of a tertiary care hospital in India. World J Adv Res Rev. 2021;11(1):081–90
21. Lino K, Guimarães GMC, Alves LS, Oliveira AC, Faustino R, Fernandes CS, et al. Serum ferritin at admission in hospitalized COVID-19 patients as a predictor of mortality. Braz J Infect Dis. 2021;25(2):101569.
22. Hong L-Z, Shou Z-X, Zheng D-M, Jin X. The most important biomarker associated with coagulation and inflammation among COVID-19 patients. Mol Cell Biochem. 2021;476(7):2877–85.
23. IwamuraAPD, Tavares da Silva MR, Hümmelgen AL, Soeiro Pereira PV, Falcai A, Grumach AS, et al. Immunity and inflammatory biomarkers in COVID-19: A systematic review. Rev Med Virol. 2021;31(4):e2199.
24. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z, et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care. 2020;8(1):49.
25. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021;41(6):540–8
26. Das B, Bhatia SY, Pal PM. Evaluation of the role of routine laboratory biomarkers in COVID-19 patients: Perspective from a tertiary care hospital in India. Indian J Clin Biochem. 2021;1–12.
27. Alonso-Fernández A, Toledo-Pons N, Cosío BG, Millán A, Calvo N, Ramón L, et al. Prevalence of pulmonary embolism in patients with COVID-19 pneumonia and high D-dimer values: A prospective study. PLoS One. 2020;15(8):e0238216
28. Hong L-Z, Shou Z-X, Zheng D-M, Jin X. The most important biomarker associated with coagulation and inflammation among COVID-19 patients. Mol Cell Biochem. 2021;476(7):2877–85.
29. Açıksarı G, Koçak M, Çağ Y, Altunal LN, Atıcı A, Çelik FB, et al. Prognostic value of inflammatory biomarkers in patients with severe COVID-19: A single-center retrospective study. Biomark Insights. 2021;16:11772719211027022.
30. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021;41(6):540–8.
31. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021;41(6):540–8.
32. Das B, Bhatia SY, Pal PM. Evaluation of the role of routine laboratory biomarkers in COVID-19 patients: Perspective from a tertiary care hospital in India. Indian J Clin Biochem. 2021;1–12.
33. Chen X, Gao W, Li J, You D, Yu Z, Zhang M, et al. A predictive paradigm for COVID-19 prognosis based on the longitudinal measure of biomarkers. Brief Bioinform [Internet]. 2021;

34. Das B, Bhatia SY, Pal PM. Evaluation of the role of routine laboratory biomarkers in COVID-19 patients: Perspective from a tertiary care hospital in India. Indian J Clin Biochem. 2021;1–12.
35. Bivona G, Agnello L, Ciaccio M. Biomarkers for prognosis and treatment response in COVID-19 patients. Ann Lab Med. 2021;41(6):540–8
36. Peckham H, Gruijter NM, et al. Male sex identified by global COVID-19 meta-analysis as a risk factor for death and ITU admission. Nature Communications2020; 11)
37. (Levi M, van der Poll T. Coagulation and sepsis. Thromb Res 2017; 149: 38–44.)
38. Lue W, Yu H, Gou J, et al. Clinical pathology of critical patient with novel coronavirus pneumonia (COVID-19). Preprints 2020; 1–18
39. Thachil, J., Tang, N., Gando, S., Falanga, A., Cattaneo, M., Levi, M., Clark, C., &Iba, T. (2020). ISTH interim guidance on recognition and management of coagulopathy in COVID-19. *Journal of Thrombosis and Haemostasis: JTH*, *18*(5), 1023–1026.
40. Yao Y, Cao J, Wang Q, Shi Q, Liu K, Luo Z et al. D-dimer as a biomarker for disease severity and mortality in COVID-19 patients: a case control study. J Intensive Care 2020;8:49
41. Zhou B, She J, Wang Y, Ma X. Utility of Ferritin, Procalcitonin, and C-reactive Protein in Severe Patients with 2019 Novel Coronavirus Disease. In: 10.21203/ rs.3.rs-18079/v1 [22 May 2020]
42. Ko JH, Park GE, Lee JY, et al. Predictive factors for pneumonia development and progression to respiratory failure in MERS-CoV infected patients. J Infect. 2016;73(5):468-475. https://doi.org/10.1016/j.jinf.2016.08.005
43. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk Factors Associated WithAcute Respiratory Distress Syndrome and Death in Patients With CoronavirusDisease 2019 Pneumonia in Wuhan, China. JAMA internal medicine. 2020;[Epub ahead of print].
44. Chen T, Wu D, Chen H, Yan W, Yang D, Chen G, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ (Clinical research ed). 2020;368:m1091.
45. Shi J, Li Y, Zhou X, Zhang Q, Ye X, Wu Z, et al. Lactate dehydrogenase andsusceptibility to deterioration of mild COVID-19 patients: a multicenter nested case-control study. BMC medicine. 2020;18(1):168.
46. Poggiali E, Zaino D, Immovilli P, Rovero L, Losi G, Dacrema A, et al. Lactate dehydrogenase and C-reactive protein as predictors of respiratory failure in